

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A method for detecting a target biopolymer in a sample, comprising:

- (a) preparing a microarray of said sample by dispensing aliquots of said sample at discrete sites onto a substrate and immobilizing said target biopolymer on said substrate, wherein the microarray is an array of dots, each dot having a diameter from about 1 to 500 microns, wherein each of said aliquots contains the same amount of said target biopolymer;
- (b) contacting said microarray with [a probe biopolymer] one or a plurality of probe biopolymers under conditions that allow the formation of [a complex] one or a plurality of complexes, each complex comprising said target biopolymer and [said probe biopolymer] one of said probe biopolymers, wherein said probe [biopolymer is] biopolymers are [applied to dots individually] deposited on said dots in said microarray; and
- (c) detecting the presence of and quantifying said [complex] complexes as a measurement for the presence or the amount of the target biopolymer in said sample.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

2. (Original) The method of claim 1, wherein the preparation of said microarray further comprises dispensing said sample aliquots on said substrate by a method selected from the group consisting of jet printing, piezoelectric dispensing methods, solenoid dispensing methods, thermal dispensing methods, solid pin contact printing methods, capillary quill contact printing methods, microfluidic-based printing, and silk screening.

3. (Original) The method of claim 1, wherein said aliquots comprise picomole amounts of said target biopolymer.

4. (Original) The method of claim 1, wherein said aliquots comprise femtomole amounts of said target biopolymer.

5. (Original) The method of claim 1, wherein said aliquots comprise attomole amounts of said target biopolymer.

6. (Original) The method of claim 1, wherein said aliquots comprise zeptomole amounts of said target biopolymer.

7. (Original) The method of claim 1, wherein said target biopolymer or said probe biopolymer is selected from the group consisting of polynucleotides, polypeptides, carbohydrates, and analogs thereof.

8. (Currently amended) The method of claim 7, wherein said polynucleotide is selected from the group consisting of amplified DNA, cDNA, single-stranded DNA, double-stranded DNA, peptide nucleic acids (PNA), RNA, and mRNA.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

9. (Original) The method of claim 7, wherein said polypeptide is selected from the group consisting of antibodies, antibody fragments, antigens, ligands, and receptors.

10. (Currently amended) The method of claim 1, wherein said target biopolymer is a first polynucleotide and said probe biopolymer is a second polynucleotide that is complementary to said [target] first polynucleotide.

11. (Original) The method of claim 1, wherein said target biopolymer is a receptor and said probe biopolymer is a ligand for said receptor.

12. (Original) The method of claim 1, wherein said target biopolymer is an antigen and said probe biopolymer is an antibody specific for said antigen.

13. (Original) The method of claim 1, wherein said probe is labeled with a reporter selected from the group consisting of dyes, chemiluminescent compounds, enzymes, fluorescent compounds, metal complexes, magnetic particles, biotin, haptens, radio frequency transmitters, radioluminescent compounds, radioactive-labeled biomolecules, dye-labeled beads, quantum dots, and bar coded particles.

14. (Original) The method of claim 1, wherein said substrate is made of crosslinked polymers, porous foam, nitrocellulose, nylon, glass, silica, ceramic, gold, porous metallic materials, non-porous metallic materials, and surface modified materials.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

15. (Original) The method of claim 14, wherein said crosslinked polymers are selected from the group consisting of polypropylene, polyethylene, polystyrene, and carboxylated polyvinylidene fluoride.

16. (Original) The method of claim 14, wherein said surface-modified materials are modified with functional groups selected from the group consisting of acyl fluoride, esters, amino, carboxyl, hydroxyl, epoxide, thiol, and alkanethiols.

17. (Original) The method of claim 1, wherein said target biopolymer is immobilized on the substrate by direct adsorption or covalent attachment.

18. (Original) The method of claim 1, wherein said support is in the form of foams, filaments, threads, sheets, films, slides, gels, membranes, beads, plates, and planar devices having discrete isolated areas in the form of wells, troughs, pedestals, hydrophobic or hydrophilic patches, die-cut adhesive reservoirs, or other physical barriers to fluid flow.

19. (Original) The method of claim 1, wherein the surface of said support is modified to contain hydrophobic and/or hydrophilic regions prior to said dispensing step.

20. (Original) The method of claim 1, wherein said substrate is wetted with an organic modifier selected from the group consisting of ethanol, methanol, isopropanol, 2-butanol, acetic acid, dextran sulfate and polyacrylic acid, prior to said dispensing step.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

21. (Previously presented) The method of claim 1, further comprising co-dispensing an internal standard with said sample to determine the concentration of said target biopolymer in said aliquots.

22. (Currently amended) The method of claim 1, wherein in step (b), said microarray is contacted with a plurality of [probes] probe biopolymers.

23. (Currently amended) The method of claim 22, wherein each aliquot is contacted with a different probe biopolymer.

24. (Currently amended) The method of claim 22, wherein said [probes] probe biopolymers are labeled with identical reporter groups.

25. (Currently amended) The method of claim 22, wherein said [probes] probe biopolymers are labeled with reporters that are distinguishable from one another.

26. (Currently amended) The method of claim 1, wherein in step (b), each of said aliquots is contacted with a plurality of [probes] probe biopolymers.

27. (Currently amended) The method of claim 26, wherein said [probes] probe biopolymers are labeled with reporters that are distinguishable from one another.

28. (Original) The method of claim 1, wherein said aliquots are deposited onto said substrate at about 1 to 1536 sites per square millimeter of the substrate surface area.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

29. (Original) The method of claim 1, wherein said substrate is a multiple well microplate, and said aliquots are deposited at between 1 to 1536 sites per well of said microplate.

30. (Currently amended) A method for detecting a target nucleic acid in a sample, comprising:

- (a) preparing a microarray of said sample by dispensing aliquots of said sample at discrete sites onto a substrate and immobilizing said target nucleic acid on said substrate, wherein the microarray is an array of dots, each dot having a diameter from about 1 to 500 microns, wherein each of said aliquots contains the same amount of said target nucleic acid;
- (b) contacting said microarray with [a] one or a plurality of labeled nucleic acid [probe] probes under hybridizing conditions that allow the formation of [a complex between] one or a plurality of complexes, each complex comprising said target nucleic acid and one of said [probe] probes, wherein said probe is a nucleic acid that is substantially complementary to said target nucleic acid, wherein said labeled nucleic acid [probe is applied to dots individually] probes are deposited on said dots in said microarray; and
- (c) detecting the presence of and quantifying said [complex] complexes as a measurement for the presence or the amount of said target nucleic acid in said sample.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

31. (Original) The method of claim 30, wherein the preparation of said microarray further comprises dispensing said sample aliquots on said substrate by a method selected from the group consisting of jet printing, piezoelectric dispensing methods, solenoid dispensing methods, thermal dispensing methods, solid pin contact printing methods, capillary quill contact printing methods, microfluidic-based printing, and silk screening.

32. (Original) The method of claim 30, wherein said aliquots comprise picomole amounts of said target nucleic acid.

33. (Canceled)

34. (Original) The method of claim 30, wherein said aliquots comprise femtomole amounts of said target nucleic acid.

35. (Original) The method of claim 30, wherein said aliquots comprise attomole amounts of said target nucleic acid.

36. (Original) The method of claim 30, wherein said aliquots comprise zeptomole amounts of said target nucleic acid.

37. (Original) The method of claim 30, wherein said target nucleic acid is selected from the group consisting of single-stranded RNA, mRNA, single-stranded DNA, double-stranded DNA, amplified DNA, cDNA and PNA.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

38. (Original) The method of claim 30, wherein said labeled probe is selected from the group consisting of single-stranded RNA, mRNA, single-stranded DNA, double-stranded DNA, amplified DNA, cDNA, and PNA.

39. (Original) The method of claim 30, wherein said probe is labeled with a reporter selected from the group consisting of dyes, chemiluminescent compounds, enzymes, fluorescent compounds, metal complexes, magnetic particles, biotin, haptens, radio frequency transmitters, radioluminescent compounds, radioactive-labeled biomolecules, dye-labeled beads, quantum dots, and bar coded particles.

40. (Original) The method of claim 30, wherein said substrate is made of crosslinked polymers, porous foam, nitrocellulose, nylon, glass, silica, ceramic, gold, porous metallic materials, non-porous metallic materials, and surface-modified materials.

41. (Original) The method of claim 40, wherein said crosslinked polymers are selected from the group consisting of polypropylene, polyethylene, polystyrene, and carboxylated polyvinylidene fluoride.

42. (Original) The method of claim 40, wherein said surface-modified materials are modified with functional groups selected from the group consisting of acyl fluoride, esters, amino, carboxyl, hydroxyl, epoxide, thiol, and alkanethiols.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

43. (Original) The method of claim 30, wherein said substrate is wetted with an organic modifier selected from the group consisting of ethanol, methanol, isopropanol, 2-butanol, acetic acid, dextran sulfate and polyacrylic acid, prior to said dispensing step.

44. (Original) The method of claim 30, further comprising co-dispensing an internal standard with said sample to determine the concentration of said target nucleic acid in said aliquots.

45. (Original) The method of claim 30, wherein in step (b), the microarray is contacted with a plurality of probes.

46. (Original) The method of claim 45, wherein each aliquot is contacted with a different probe.

47. (Original) The method of claim 45, wherein each probe is labeled with an identical reporter.

48. (Original) The method of claim 45, wherein said probes are labeled with reporters which are distinguishable from one another.

49. (Original) The method of claim 30, wherein each of said aliquots is contacted with a plurality of probes.

50. (Original) The method of claim 49, wherein said probes are labeled with reporters which are distinguishable from one another.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

51. (Original) The method of claim 30, wherein said aliquots are deposited onto said substrate at about 1 to 1536 sites per square millimeter of the substrate surface area.

52. (Original) The method of claim 30, wherein said substrate is a multiple well microplate, and said aliquots are deposited at between 1 to 1536 sites per well of said microplate.

53. (Currently amended) A method for identifying one or more target analytes in a sample, comprising:

- (a) preparing a microarray of said sample by dispensing aliquots of said sample at discrete sites onto a substrate and immobilizing said analytes on said substrate, wherein the microarray is an array of dots, each dot having a diameter from about 1 to 500 microns, wherein each of said aliquots contains the same amount of said target analytes;
- (b) contacting said microarray with a plurality of labeled probes specific for each of said target analytes under conditions that allow formation of a [complex between each] plurality of complexes, each complex comprising one of said target analytes and one of said labeled [probe] probes specific for said target analyte, wherein said plurality of labeled probes are [applied to dots individually] deposited on said dots in said microarray; and
- (c) detecting and quantifying said complexes as a measurement of the presence or the amount of said target analytes.

54. (Original) The method of claim 53, wherein the preparation of said microarray further comprises dispensing said sample aliquots on said substrate by

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

a method selected from the group consisting of jet printing, piezoelectric dispensing methods, solenoid dispensing methods, thermal dispensing methods, solid pin contact printing methods, capillary quill contact printing methods, microfluidic-based printing, and silk screening.

55. (Original) The method of claim 53, wherein said analyte is selected from the group consisting of biopolymers, drugs, small organic molecules, nucleic acids, proteins, receptors, antigens, carbohydrates, cells, cellular fragments, and tissues.

56. (Original) The method of claim 53, wherein said probe is selected from the group consisting of nucleic acids, antibodies, antibody fragments, ligands, and carbohydrates.

57. (Original) The method of claim 53, wherein said label is selected from the group consisting of dyes, chemiluminescent compounds, enzymes, fluorescent compounds, metal complexes, magnetic particles, biotin, haptens, radio frequency transmitters, radioluminescent compounds, radioactive-labeled biomolecules, dye-labeled beads, quantum dots, and bar coded particles.

58. (Original) The method of claim 53, wherein said aliquots comprise picomole amounts of said analyte.

59. (Original) The method of claim 53, wherein said aliquots comprise femtomole amounts of said analyte.

60. (Original) The method of claim 53, wherein said aliquots comprise attomole amounts of said analyte.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

61. (Original) The method of claim 53, wherein said aliquots comprise zeptomole amounts of said analyte.

62. (Original) The method of claim 53, wherein said substrate is made of crosslinked polymers, porous foam, nitrocellulose, nylon, glass, silica, ceramic, gold, porous metallic materials, non-porous metallic materials, and surface-modified materials.

63. (Original) The method of claim 53, wherein said surface-modified materials are modified with functional groups selected from the group consisting of acyl fluoride, esters, amino, carboxyl, hydroxyl, epoxide, thiol, and alkanethiols.

64. (Original) The method of claim 53, wherein the surface of said support is modified to contain hydrophobic and/or hydrophilic regions prior to said dispensing step.

65. (Original) The method of claim 53, wherein said substrate wetted with an organic modifier selected from the group consisting of ethanol, methanol, isopropanol, 2-butanol, acetic acid, dextran sulfate and polyacrylic acid, prior to said dispensing step.

66. (Original) The method of claim 53, further comprising co-dispensing an internal standard with said sample to determine the concentration of said analytes in said aliquots.

67 (Original) The method of claim 53, wherein each aliquot is contacted with a different probe.

Application Serial No. 09/945,145
Customer No.: 26021
Reply to Office Action Dated 07/29/04

PATENT
1984-045 (81841.0145)

68. (Original) The method of claim 67, wherein each probe is labeled with an identical reporter.

69. (Original) The method of claim 67, wherein each probe is labeled with a different reporter.

70. (Original) The method of claim 53, wherein each aliquot is contacted with a plurality of probes.

71. (Original) The method of claim 53, wherein said aliquots are deposited onto said substrate at about 1 to 1536 sites per square millimeter of the substrate surface area.

72. (Original) The method of claim 53, wherein said substrate is a multiple well microplate, and said aliquots are deposited at between 1 to 1536 sites per well of said microplate.